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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,956	11/20/2003	Xue Mei Zhou	3527.1	3639

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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/22/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,956	ZHOU, XUE MEI	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-12* is/are pending in the application.

4a) Of the above claim(s) *7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, and 4-12 are pending.
Claims 2, 3, and 13-16 are cancelled.
Claims 7-12 are withdrawn
Claims 1, and 4-6 are examined on the merits

This Office Action is in reply to Applicants' correspondence of 09/21/2006. Claims 13-16 have been cancelled; claims 7-12 are withdrawn; no claims have been newly added; claim 1 has been amended. Applicants' remarks and amendments have been fully considered but are not found to be persuasive.

No new grounds of rejection are presented in this Office Action. Any rejections or objections not reiterated herein have been withdrawn.

This Action is made FINAL.

Specification

1. Applicant has addressed an objection to the specification by providing a paragraph to replace the paragraph beginning on page 25 line 4. It is noted that this replacement paragraph recites 'an array comprising SEQ ID Nos: 1-688,466'. Applicant should ensure that the replacement paragraph is written as intended, as other parts of the specification describe an array of SEQ ID NO: 1-699-466.

Withdrawn Claim Rejection - 35 USC § 101

2. The rejection of claims under 35 USC 101 for lack of utility is WITHDRAWN in light of Applicants arguments that the claims are drawn to a probe set that can be used in the analysis of rat gene expression and that the probe set has substantial use, as evidenced by Weaver et al (2006) and Stuart et al (2001), in the study of gene expression related to specific phenotypes.

Claim Rejections - 35 USC § 112 1st ¶ Written Description

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 4-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

> Applicant is referred to the revised interim guidelines on written description published January 5, 2001 in the Federal Register, Volume 66, Number 5, page 1099-111 (also available at www.uspto.gov <http://www.uspto.gov>).

The claims are drawn to arrays of nucleic acid probes derived from rat genomic sequences. Claims 1 and 4-6 are drawn to arrays in which the probes consist essentially of SEQ ID NOs: 1-699,466.

When the claims are analyzed in light of the specification, the instant invention encompasses an enormous number of nucleic acid probes comprising a wide variety of nucleic acid sequences. The claims are drawn to a plurality of nucleic acid probes that encompass an extremely large genus of full length genes, cDNAs, and variants (splice variants, polymorphisms and mutations including single and multiple nucleotide substitution, insertions, deletions, translocations and gene rearrangements). For claims 1 and 4-6, the claimed probes need only minimally comprise the recited 25 mers. Thus, while the disclosure teaches SEQ ID NO: 1-699,466, each disclosed SEQ ID NO is a

unique fragments of the rat genome; and the claims encompass probes wherein each probe 'consists essentially of' the disclosed SEQ ID NOs, which includes any nucleic acids containing any sequence additional to the disclosed SEQ ID NOs, such as, for example, full transcripts containing polymorphisms and mutations not taught by the instant specification. Nucleic acids of such a large genus have not been taught by the specification.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. The sequence listing of the instant application provides only SEQ ID NOs: 1-699,466. While the specification teaches that each of the disclosed sequences corresponds to and represents at least four additional nucleic acid sequences with one or more mismatches located anywhere in the disclosed sequences, the instant application does not provide any SEQ ID NOs other than SEQ ID NOs: 1-699,466.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the specification does not provide any characteristics other than the nucleic acid sequences of SEQ ID NOs: 1-699,466.

Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ

> 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In the instant application, with the exception of an array comprising nucleic acid probes wherein each probe consists of one of SEQ ID NOs: 1-699,466, one of skill in the art cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required.

In conclusion, the limited information provided regarding SEQ ID NOs: 1-699,466 is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of polynucleotide sequences besides those particularly disclosed in the specification at the time the application was filed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

Response to Remarks

5. Applicants have argued that claim 1 has been amended to replace the transitional phrase 'comprising' with the more limited scope transitional phrase 'consists

essentially of' (Remarks page 10). However, the MPEP (see section 2111.03 – Transitional phrases) indicates that:

> A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco, Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

In the instant case, while the Remarks argue that the claims are drawn to 'an array of 699,466 twenty-five base probes' (Remarks p.8, last ¶), and that 'probes are no longer that 25 base in length and have the sequences of one of the sequences in the sequence listing without additional flanking sequence', because the specification does not clearly indicate that the 'consisting esseintially of' language is the same as the 'consisting of' language, the transitional phrase of the instant claims is interpreted as equivalent to 'comprising'. See for example the instant specification page 12 for the definition of 'array' as including nucleic acids of essentially any length, and page 18 where it is stated that 'the present invention includes...longer nucleotide sequences which include the nucleic acid sequences listed in SEQ ID NO: 1-699,466'.

Additionally, Applicants' arguments in the Remarks (page 8, last ¶) indicate that the particular array of twenty-five base probes of SEQ ID NO: 1-699,466 individually, reproducibly, and accurately interrogate the expression level of a collection of more than 20,000 rat genes simultaneously without inter-gene cross hybridization. However, as stated above, the 'consists essentially of' language allows for the addition of unspecified nucleotides to any probe, where the specification does not provide any guidance as to

how one might a priori identify any probes other than probes consisting of SEQ ID NO: 1-699,466 that are suitable to function together to give optimal performance under a specified set of hybridization conditions, as argued in the Remarks (p.9, lines 3-5).

The rejection is MAINTAINED.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 4, and 6, are rejected under 35 U.S.C. 102(b) as being anticipated by Gunther et al (1985).

Gunther et al teaches a Southern blot of rat genomic DNA on a nitrocellulose membrane.

Regarding claim 1, Gunther et al teaches a blot that contains genomic DNA isolated from rat liver (p.1258 – DNA preparation), digested with restriction enzymes, and transferred onto nitrocellulose (p.1258 – Restriction enzyme digestion, gel electrophoresis, blotting, and hybridization). The resulting membrane (Fig 2; Fig 3) thus contains a plurality of nucleic acid probes (the various restriction fragments) corresponding to the entire rat genome. Because of the comprehensive nature of the probes on the blot taught by Gunther et al (i.e. the blot is the entire rat genome), the plurality of probes on the southern blot inherently consist essential of each of the

sequences listed in SEQ ID NO: 1-699,466, which are taught by the instant specification to be derived from rat genes.

Regarding claims 4 and 6, Gunther et al teaches a blot on nitrocellulose, which is a solid support. The reference further teaches that the genomic DNA from a rat is separated in a single lane of a gel and transferred to the nitrocellusoe, thus the separated probes are on a single contiguous solid support (Fig 2; Fig 3).

Response to Remarks

Applicant has traversed the rejection of claims under 35 USC 102 as anticipated by Gunther et al. Applicants argue that the claims require that the probes of the claimed array are all 25 bases and each sequence is a separate probe. This argument has been fully and carefully considered but is not found to be persuasive. The claims do not require 699,466 individual probes where each probe consitst of one of SEQ ID NO: 1-699,466. The claims require only an array comprising 'a plurality of probes' wherein each probe 'consists essentially of one of the sequences listed in SEQ ID NO: 1-699,466' and the total array comprises each of SEQ ID NO: 1-699,466. As discussed in the Response to Remarks above, the language of 'consists essentially of' does not limit the probes to only the 25-mer sequences listed in the sequence listing of the instant specification. For example and array of three probes, where the first probe contains the contiguous nucleotide sequences of SEQ ID NO: 1-233,155, the second probe contains the contiguous nucleotide sequences of SEQ ID NO: 233,156-466,310, and the third probe contains the contiguous nucleotide sequences of SEQ ID NO:

466,311-699,466 would satisfy all of the limitations of the claims; such an array would be a plurality of probes, each probe would 'consist essentially of' one of the sequence of SEQ ID NO: 1-699,466, and the plurality of probes would comprise each of the sequences listed as SEQ ID NO: 1-699,466.

The rejection is MAINTAINED.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rat UniGene Build 99 (June 2002) in view of Fodor et al US Pat 6,309,822 (as cited in the IDS).

The claims are drawn to arrays of nucleic acid probes. Claims 1 and 4-6 are drawn to arrays of probes wherein the probes consist essentially of SEQ ID NO: 1-699,466. Claim 4 requires that the probes are attached to a solid support, claim 5 requires that the probes are attached to beads, and claim 6 requires that the array consist of a single contiguous solid support.

Rat UniGene Build 99 (as disclosed in the Data Sheet for Affymetirx Rat Genome 230 Arrays, page 2) teaches the sequences of genes and ESTs from rat. Build 99

teaches sequences information regarding greater than 24,000 mRNA. Absent evidence to the contrary, the Build 99, is taken to provide the sequence information of SEQ ID NOS 1-699,466 (relevant to claims 1, and 4-6). The UniGene database does not teach probes comprising each of SEQ ID NOs 1-699,466.

Fodor teaches arrays of oligonucleotide probes for gene expression analysis (col 2).

Regarding claim 1, Fodor teaches that the array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm^2, wherein sets of probes are chosen to be complementary over a gene sequence (col. 14). The reference teaches that particularly preferred probes have lengths from about 20 to about 25 nucleotides in length, and has multiple oligonucleotide probes complementary to each gene (col. 3)

Regarding claims 4 and 5, Fodor teaches that the oligonucleotides in the array can be provided attached to beads (col. 21), including individual probes attached to each bead.

Regarding claim 6, Fodor et al teaches that probe density of an array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm^2.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the gene and EST sequence information of Rat UniGene Build 99 to have constructed nucleotide probe arrays as taught by Fodor et al. Such an array would have included probe sets for genes and ESTs in the

UniGene database for the purpose of providing an array of probes for gene expression analysis as taught by Fodor. The ordinary artisan would have been motivated to provide an array of probe sets for rat sequences because Fodor teaches arrays for gene expression monitoring.

It is noted that the specification of the instant application indicates that the probes of the instant invention are derived from the Rat UniGene database (build 99) (page 32).

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 103 as obvious over Rat Unigene build 99 in view of Fodor. Applicants argues that probes consisting of SEQ ID NO: 1-699,466 are a unique set that were carefully selected to function together, and that the choice of the particular probes consisting of SEQ ID NO: 1-699,466 depends on numerous criteria such as hybridization behavior secondary structure, propensity for cross hybridization, target preparation methods and manufacturing considerations (Remarks page 15). The argument has been fully considered but is not found to be persuasive.

As noted in the Responses above, the instant claims are drawn to an array comprising probes wherein each probe 'consists essentially of one of the sequences listed in SEQ ID NO: 1-699,466. The claims do not require probes 'consisting' of SEQ ID NO: 1-699,466, where the arguments are drawn to such probes. Thus applicants arguments concerning the particular functionality of twenty-five base probes where each probes consists of one of SEQ ID NO: 1-699,466 is not applicable to the currently

claimed subject matter. Thus the examiner maintains that in light of the data presented in the Rat Unigene build 99 and the teachings of Fodor, one of ordinary skill in the art would have been motivated to use any and all of the Unigene data to create an array of probes wherein each probe 'consists essentially of' one of SEQ ID NO: 1-699,466 and the total array comprise each of the sequences of SEQ ID NO: 1-699,466.

Conclusion

10. No claim is allowable. No claim is free of the prior art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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